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THE LOCAL INFLAMMATORY REACTION PRODUCED BY THE TETANUS BACILLUS

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A review of recent literature and of standard books of pathology has not revealed a description of the reaction of the tissues to the presence of the bacillus of tetanus. Therefore the experimental production of tetanus in guinea-pigs was undertaken to study the reaction of the tissues at the site of inoculation to the tetanus bacillus.

In the production of the disease were used pure cultures of a strain of B. tetanus known to be virulent to guinea-pigs. This strain was secured from Dr. E. M. Houghton of Parke, Davis & Company of Detroit. Injections were made of actively growing cultures 72 hours old, so that few if any spores were introduced. Injections of cultures in fluid medium produced almost immediate symptoms because of the toxin present, and this method had to be abandoned and injections made of suspensions in salt solution of tetanus bacilli grown on the surface of solid medium. The cultures were incubated in a chamber of hydrogen gas; later a chamber freed of oxygen by pyrogallic acid and sodium hydrate was substituted. The dose was 0.25 c c of a suspension of standard turbidity and of sufficient strength to produce tetanus in guinea-pigs of 250 to 300 gm. The sites for the injections were the subcutaneous and muscular tissues of the right thigh and also the foot pad. In the former some of the bacilli reached the thigh muscles so that muscle cell reactions could be observed, and in the second the site of local disease was the same as the site of inoculation frequently encountered in tetanus in human beings. Studies were made of serial microscopic sections of the lesions, made at intervals from 12 hours after inoculation up to several days after the appearance of generalized tetanus.

All animals from which lesions were studied presented symptoms of tetanus in nearly all instances as early as about 12 hours after the injection. A definite rigidity of the muscles of the injected extremity, the so-called "local tetanus," was observed first. After a few hours the

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opposite extremity commonly became rigid and finally the whole body was involved—"ascending tetanus"—with opisthotonus, convulsions, and trismus.

Microscopic examination in the early stages of the disease, that is about 12 hours after the inoculation, revealed an intense cellular invasion of the affected area. The site of local reaction was pretty sharply defined by the cellular invasion. Definite necrosis or abscess formation did not develop. The predominating cell in the early stage was the polymorphonuclear leukocyte which makes up about 80 to 90% of the cells present. In addition a few mononuclear leukocytes and large mononuclear wandering cells are present. The capillaries are engorged and the endothelial cells are enlarged so that they project into the lumen of the vessel (fig. 1). There is also a distinct perivascular infiltration of inflammatory cells. The bacilli occur chiefly in clumps

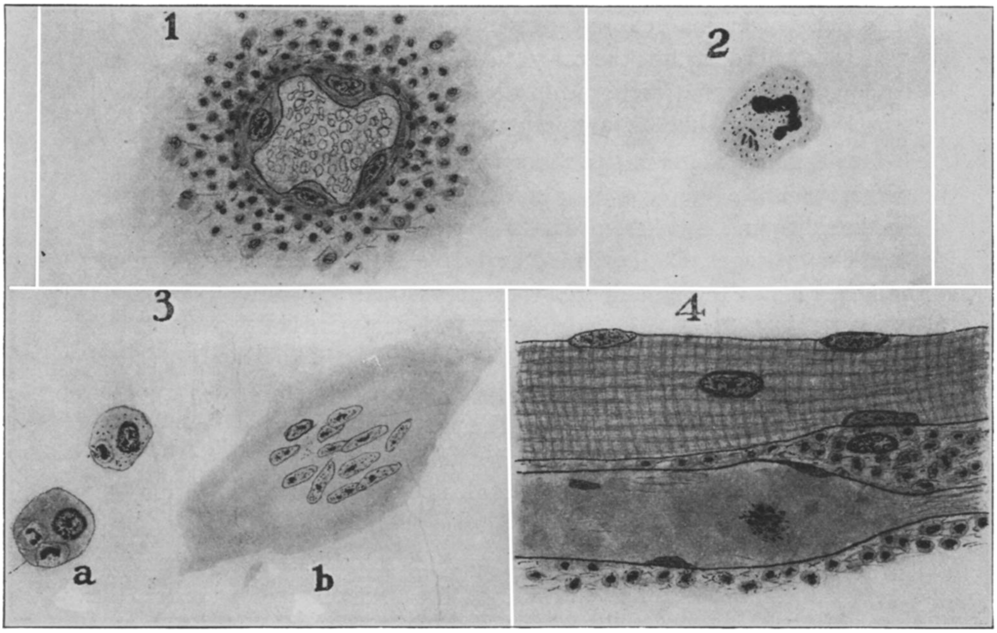

Fig. 1.—Hyperplasia of endothelial cells in the capillary wall.
Fig. 2.—Polymorphonuclear leukocyte with four tetanus bacilli.
Fig. 3.—Leukocytes engulfed by mononuclear cell (*a*) and giant cell (*b*).
Fig. 4.—Disintegration of nucleus of muscle cell and waxy change of muscle (van Gieson stain).

scattered in the spaces between the leukocytes and fixed cells. A few bacilli, however, are seen within polymorphonuclear leukocytes (fig. 2) indicating that tetanus bacilli exert a positive chemotaxis, which is in agreement with Werigo[1] who doubted that any virulent bacteria would exert a negative chemotaxis on leukocytes, as claimed by some and recently by Metalnikow.[2] Some of the polymorphonuclear leukoctyes are engulfed by large mononuclear wandering cells, as shown in fig. 3. At this stage no hyaline or waxy change has taken place in the muscle, but the nuclei in the sarcolemma are swollen. No foreign body giant cells and no plasma cells are present, and there is no hyperplasia or increase of fibroblasts in the early stages. The alveolar tissue is invaded by large numbers of cells as is the loose fibrous tissue between the muscle bands, so that the latter are widely separated.

In the older lesions polymorphonuclear leukocytes become less numerous while lymphocytes and mononuclear wandering cells increase so that they make up from one-half to one-third of the cells present. In the later stages, that is, after 5 or 6 days, large fibroblasts are present and the reparative phase of the reaction is now established. The muscle cells are also affected as evidenced by disappearance of the striations, granular disintegration of nuclei (fig. 4), and the presence of a well defined waxy degeneration. The formation of giant cells is another characteristic of the later stages of the reaction; they mingle with other cells, and their nuclei are centrally located (fig. 3). Plasma cells have not been found in any of the microscopic preparations of lesions of even several days' duration.

In connection with these observations, microscopic studies were made also of the local lesion in the sole of the foot obtained, through the courtesy of Dr. E. R. LeCount, postmortem from the body of a man who died from tetanus. While no conclusions are drawn from this single examination of human material, it may be noted that the cellular invasion, the hyperplasia of fibroblasts, and the inflammatory reaction generally corresponded in all essentials to the changes observed in the older experimental lesions.

SUMMARY

When typical tetanus is produced in guinea-pigs by injection into the thigh muscles and foot pads of suspensions of tetanus bacilli, an

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[1] Ann. de L'Inst. Pasteur, 1894, 8, p. 1.

[2] Ibid., 1921, 35, p. 363.

intense inflammatory reaction promptly ensues at the site of inoculation, in which both wandering and fixed cells take part.

The tetanus bacillus exerts a positive chemotaxis and is taken up by polymorphonuclear leukocytes; it also induces the formation of giant cells.

In one human case the local reaction to the tetanus bacillus corresponded in all essentials to the reaction of experimental inoculation in guinea-pigs.